A systems biology approach for defining the molecular framework of the hematopoietic stem cell niche.

Journal: Cell Stem Cell

Publication Year: 2014

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PubMed link: 25042701

Funding Grants: DECIPHERING THE INSTRUCTIONS FOR VERTEBRATE HSC SPECIFICATION AND AMPLIFICATION.

Public Summary:
Despite progress in identifying the cellular composition of hematopoietic stem/progenitor cell (HSPC) niches, or their local micro environments, little is known about the molecular requirements of HSPC support. To address this issue, we used a panel of six recognized HSPC-supportive stromal lines and less-supportive counterparts originating from embryonic and adult hematopoietic sites. Through comprehensive analyses of the genes each expresses, we identified 481 mRNAs and 17 microRNAs organized in a modular network implicated in cell to cell signaling. Importantly, this network of gene expression could predict whether or not previously uncharacterized stromal lines could support HSPC function. This gene set contains most known HSPC regulators as well as a number of unexpected ones, which we have validated by functional studies in zebrafish embryos. In sum, our approach has identified the core molecular network required for HSPC support. These cues, along with a searchable web resource, will inform ongoing efforts to instruct HSPC ex vivo amplification and formation from pluripotent precursors.

Scientific Abstract:
Despite progress in identifying the cellular composition of hematopoietic stem/progenitor cell (HSPC) niches, little is known about the molecular requirements of HSPC support. To address this issue, we used a panel of six recognized HSPC-supportive stromal lines and less-supportive counterparts originating from embryonic and adult hematopoietic sites. Through comprehensive transcriptomic meta-analyses, we identified 481 mRNAs and 17 microRNAs organized in a modular network implicated in paracrine signaling. Further inclusion of 18 additional cell strains demonstrated that this mRNA subset was predictive of HSPC support. Our gene set contains most known HSPC regulators as well as a number of unexpected ones, such as Pax9 and Ccdc80, as validated by functional studies in zebrafish embryos. In sum, our approach has identified the core molecular network required for HSPC support. These cues, along with a searchable web resource, will inform ongoing efforts to instruct HSPC ex vivo amplification and formation from pluripotent precursors.